Kidney International, Vol. 51 (1997), pp. 2018–2021

Blood transfusion during heparin-free hemodialysis

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The routine practice of hemodialysis requires anticoagulation to prevent thrombosis in the extracorporeal circuit [1, 2]. Heparin is used as the anticoagulant in the vast majority of treatments. In patients at risk of bleeding, techniques to avoid anticoagulation have been developed. These techniques include heparin free protocols using rapid blood flow and saline flushes [3–7], and various techniques for regional anticoagulation including citrate and prostacyclin regional anticoagulation [8–15].

We and others have described techniques for heparin-free hemodialysis [3–7]. In our 1989 study, we were successful in hemodialyzing 91% of hospitalized patients with significant bleeding risks without the use of anticoagulants. Less than 2% of these patients thrombosed their hemodialysis circuit and only 7% required very low dose ($< 1000\ \mu$) heparin during this protocol. However, we and others noted that blood transfusion through the hemodialysis circuit dramatically increased the likelihood of extracorporeal thrombosis [1–3]. Thus, protocols for heparin-free hemodialysis requiring fast blood flows and saline flushes have prohibited transfusion during the dialysis treatment through the dialysis circuit [1–3]. Given that large numbers of acutely bleeding patients require blood transfusions, we have worked to develop a technique to modify our heparin-free hemodialysis protocol so transfusions can be safely performed via the hemodialysis circuit without compromising the hemodialysis treatment. In addition, intravenous accesses are often a limiting factor in acutely ill patients and the ability to transfuse through the dialysis circuit while providing simultaneous ultrafiltration improves patient care. This study describes our experience with a modification of our heparin-free hemodialysis protocol that allows transfusion through the hemodialysis circuit.

Methods

Twenty-seven consecutive inpatients, who required transfusion while requiring heparin-free hemodialysis, were studied during the period of January through September 1996. The demographics of the patient population is described in Table 1. No patient who required transfusion and heparin free hemodialysis was excluded from this protocol. All patients were in the high or very high risk of bleeding group using the classification devised by Swartz and Port [16]. The location where the patient received the therapy (in the intensive care unit or in the acute hemodialysis unit), the artificial kidney employed, and the access used, are described in Table 1.

All patients received blood transfusions while dialyzed without heparin. Hemodialysis without anticoagulation was performed using the standard protocol as described at our center in 1987 [3]. Briefly, the protocol required that the artificial kidney and blood line be flushed for 10 to 15 minutes with one liter of 0.9% saline containing 3000 units of heparin. Heparin was then flushed from the dialyzer and the blood lines with at least one liter of 0.9% saline solution before blood flow was initiated. In this manner heparin was always displaced prior to the initiation of hemodialysis. Commonly used measures of anticoagulation in the extracorporeal and systemic circulation [prothrombin time (PT) and (activated thromboplastin time (PTT)] did not change pre-, during, or post-hemodialysis [3]. Blood flows of more than 250 ml/min were established rapidly and maintained at this level. When possible, blood flows were kept between 300 and 350 ml/min. Systolic blood pressure was maintained at > 100 mm Hg by the use of fluid replacement or vasopressors, as clinically indicated. Venous and arterial pressure monitors were used in all instances and were carefully monitored to detect extracorporeal thrombosis. The artificial kidney was flushed with 50 ml of 0.9% saline every 15 to 30 minutes to detect any signs of partial clotting and to prevent hemoconcentration. Partial clotting could usually be detected by either increments in the venous pressure or decreases in the arterial pressure monitor readings, or by the detection of fibrin stranding either in the kidney or in the blood drip chambers. If partial clotting could not be resolved with saline flushes, the patient received a low dose heparin regimen. This method involved administering 500 units of heparin systemically every 15 to 30 minutes with a maximum of 1,500 units per treatment. One-to-one or one-to-two nursing was characteristically used in conjunction with this technique.

Patients were assigned to receive blood transfusion during hemodialysis on the sole basis of having indication for transfusion and having a high or very high risk for bleeding using the classification system of Swartz and Port [16]. The attending nephrologist and the managing physician determined the requirement for transfusion and heparin free hemodialysis. The study team was not involved in the decision as to whether transfusion or heparin free hemodialysis was required. The time required per transfusion of packed red blood cells was 30 to 60 minutes of dialysis time. The only modification to the standard dialysis treatment was the introduction of a sterile three-way stopcock into the blood flow path (Fig. 1). This sterile stopcock was placed between the distal extreme of the dialysis venous circuit tubing and the standard extension tubing from the access needle or the

Received for publication October 7, 1996
and in revised form December 16, 1996
Accepted for publication December 16, 1996

Table 1. Patients

	Number	%
Age	55.4 ± 14.5	
Gender		
male	14	52
female	13	48
Location		
ICU	20	50
Acute HD unit	20	50
Access		
DialysisCath. (non-cuffed)	19	47.5
Permcath™ (cuffed cath)	12	30
PTFE	6	15
Tesio Cath™ (cuffed cath)	1	2.5
AVF	2	5
Filters		
HG500	27	67.5
A500	8	20
HG400	2	5
A700	2	5
F20	1	2.5
Indication for no heparin		
Recent surgery	19	
Recent bleeding	10	
Suspected aneurysm	2	
Other	9	

hemodialysis catheter (Figs. 1 and 2). Access needles were 15 gauge in all instances of AV access. Hemodialysis catheters used are described in Table 1.

A stopcock with large diameter channels and Luer locks was used to facilitate blood flow and to prevent any unsuspected detachment in this circuitry (Figs. 1 and 2). The proper positioning and attachments are depicted in Figure 1. The operator had to be certain that the device flowed in three ways simultaneously by twisting the lock valve 180 degrees away from the side port position (Fig. 1). In this manner the blood ran in a straight line through the stopcock and the blood infusion was able to come from the side port (Figs. 1 and 2). The arrows present on the stopcock guided the operator regarding flow direction (Figs. 1 and 2). The arrows must be perfectly aligned with the circuitry access to guarantee the path of minimal resistance to the bloodstream. Once the device had been safely placed, the dialysis was commenced and ran on a standard basis. Venous and arterial dialysis pressures were followed carefully from the extracorporeal circuit. Baseline pressures at 300 ml/min were compared with those while transfusing at 300 ml/min. An increase in venous pressure was expected due to the blood infusing under pressure in the positive pressure venous side. If a substantial (> 80 mm Hg) increase in venous pressure was encountered, the venous access circuit was analyzed for errors in stopcock placement and arrow alignment, catheter kink or clotting in the hemodialysis circuit or problems with venous inflow.

The transfusion circuitry was the standard transfusion equipment that connected to the described stopcock (Figs. 1 and 2). In order to facilitate transfusion, one of two maneuvers may be required to transfuse into this high pressure venous circuit: (1) The blood transfusion bag could be placed one meter above the patient to develop sufficient pressure gradient to enter this inflow circuit; or (2) A pressure bag could be attached to the transfusing blood unit and increased up to 300 mm Hg as necessary to facilitate blood entry. The transfusion line was locked at the end of each transfusion by rotating the stopcock handle to close the flow from the transfusion circuit to prevent retrograde flow. If retrograde flow occurred during transfusion with the blood elevated 1 meter above the patient the stopcock was closed and the pressure bag applied. Twenty milliliters or less of blood were expected to remain in the transfusion circuit. It is essential that the transfusion bag not be vented, as it is possible that air may enter the system.

All hemodialysis was performed using a COBE Centry3 hemodialysis machine. Artificial kidneys (Filters) were either hemophane 0.9 to 1.1 meter squared hollow fiber (HG 400, 500), or a cuprophane parallel plate 1.1 and 1.3 square meter, (Alpha 500 or 700) or an AN69 2.0 meter^2 hollow fiber (Filtral 20, F-20); all of these from Cobe Renal Care (Lakewood, CO, USA; Table 1). Hemodialysis frequency was three to five times per week for an average of three to four hours per session. A bicarbonate bath with a sodium concentration varying between 140 to 148 was used with dialysate flows of 600 ml/min and blood flows between 250 and 400 ml/min.

Results

Twenty-seven consecutive inpatients, requiring transfusion during 40 heparin-free hemodialysis, were entered into this study between January and September 1996. All sessions were carried out in intensive care units or the acute dialysis unit at DUMC (Table 1). Eleven patients were transfused more than once. Eighty units of packed red blood cells were transfused. Each patient received from 1 to 3 units, with an average of 2 units per dialysis session. The mean blood flow and the mean duration of hemodialysis were 300 ml/min and three hours, respectively. All patients who needed transfusions of blood during heparin free hemodialysis were included (Table 2).

The standard protocol for no heparin dialysis was followed without any alterations except for the inclusion of the described stopcock at the venous outflow port. Of the 40 consecutive treatments, all 40 were completed without conversion to low dose heparin. There were no clotting episodes of the extracorporeal circuit, and no treatments were terminated early. Patient coagulation parameters defined by prothrombin time (PT) and activated partial thromboplastin time (APTT) were normal prior to and after 36 of 40 treatments. Four treatments were performed in patients with a coagulopathy as defined by PT and APTT elevated pre-treatment. Venous outflow pressure increased above the pre-transfusion baseline by a mean of 30 mm Hg (Table 2). This elevation in venous outflow pressure characteristically returned to baseline when the transfusion was completed. Thirty-two treatments were delivered via a temporary hemodialysis catheter, either in the internal jugular, or the femoral position. When hemodialysis catheters were used a saline pressure bag infusion system rather than heparin was used to maintain catheter patency. Eight treatments were done via an arteriovenous access, either by an AV graft [6] or AV fistula (Table 1) [2].

Discussion

The routine practice of hemodialysis requires systemic anticoagulation to prevent thrombosis in the extracorporeal blood circulation [1, 2]. Heparin remains the most commonly used anticoagulant. Bleeding is a major complication associated with hemodialysis, especially in hospitalized patients predisposed to bleed as a result of surgery, trauma, previous bleeding or already demonstrating active bleeding. Controlled trials evaluating the

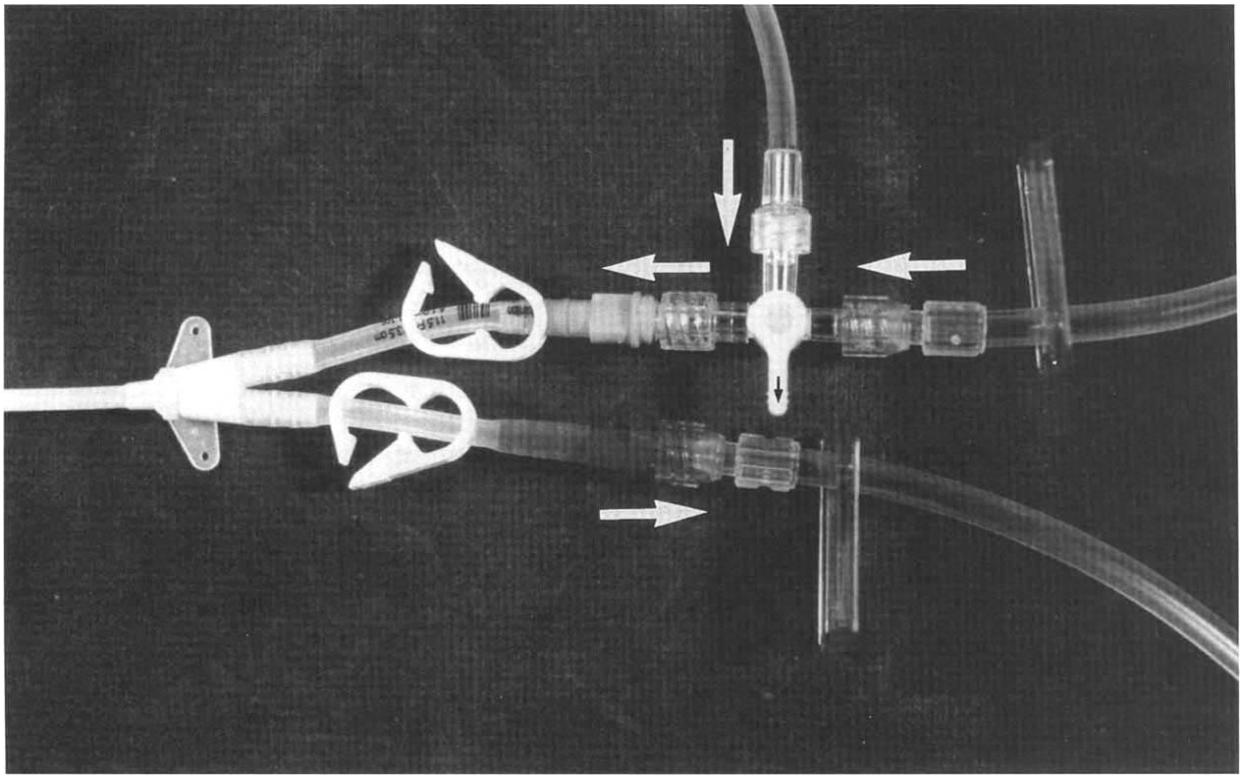

Fig. 1. *Hemodialysis circuit schematic showing the three-way stopcock attached to dialysis catheter and blood tubing with luer lock connectors.* White arrows demonstrate the direction of blood flow in the circuit and direction of blood transfusion. The black arrow demonstrates the position of the three-way stop cock handle to allow blood transfusion and hemodialysis.

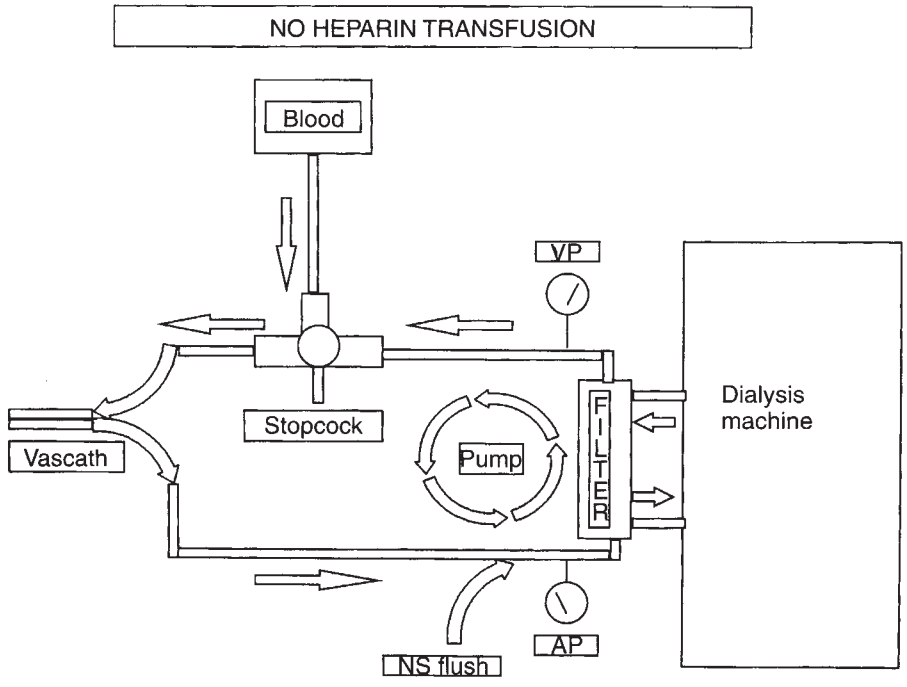

Fig. 2. *Transfusion and dialysis circuit showing direction of transfusion and blood flow.*

effectiveness of protamine regional anticoagulation versus low dose systemic heparinization have been completed [16]. Swartz and Port demonstrated that low-dose systemic heparin anticoagulation produced fewer bleeding episodes than protamine regional anticoagulation [16]. Nonetheless, significant bleeding complications were described in their study. Difficulties in the appropriate dose of protamine and the dissociation of the heparin protamine complex by the reticuloendothelial system after hemodialysis (rebound bleeding) were the proposed reasons for failure of protamine regional anticoagulation to be successful [16].

Table 2. Results

Patients	27
Blood	
Number of units	80
Range	1–3
Mean PRBC/patient	2
Venous Dialysis Pressures (VDP)	
VDP pre-transfusion	246 ± 79
VDP post-transfusion	281 ± 51
Mean VDP incr. mm Hg	30
Range *mm Hg*	(−70)–(+126)
Dialysis	
QB ml/min *mean*	300
Range *ml/min*	250–400
Mean duration *hours*	3
Range *hours*	1.5–4
% Convert/heparin	0%

Alternate agents for regional anticoagulation have included citrate and prostacyclin [8–15]. Morita and colleagues first described the technique of regional anticoagulation using citrate [18]. Subsequent modifications by Pinnick, Wiegmann and Diederich [13], Von Brecht and colleagues [15], and a prospective trial by Flannigan and associates [14] showed the utility of citrate regional anticoagulation. Complications with citrate regional anticoagulation include hypocalcemia, hypercalcemia and citrate toxicity. Some of these complications were initially described by Kelliher and Schulman [17]. Regional anticoagulation using prostacyclin has been reported [17]. Prostacyclin inhibits platelet activation without affecting the intrinsic clotting system and has a physiologic half-life of approximately five minutes. Prostacyclin's principle side effects include its potent vasodilatory properties and associated nausea and vomiting, and facial flushing. These complications have limited the application of this technique [12].

Heparin free hemodialysis has emerged as the most common technique for dialyzing patients at risk of bleeding. Glaser et al were the first in reporting successful performance of heparin-free dialysis [7]. Investigators at the University of Alabama [4] and Duke University [3], further modified and developed these techniques for heparin free dialysis. We and others have reported successful hemodialysis without the use of anticoagulation in > 91% of patients employed while maintaining hemodialysis efficiency. The principle drawback of this technique has been the inability to transfuse simultaneously through the hemodialysis circuit. It has been reasoned that the increased clotting seen with this technique and transfusion has been mediated by hemoconcentration when blood is transfused through the hemodialysis circuit. This is a significant drawback of this dialysis technique.

We reasoned that if one could place the blood infusion port distal enough in the venous circuit and infuse it under pressure, since the blood was not passing through either the artificial kidney or the drip chamber, the hemoconcentration would not increase extracorporeal thrombosis. We also reasoned that if problem developed with access flow, it would be readily detected by carefully monitoring the venous outflow pressures.

In this study we have successfully shown that 27 consecutive patients could be transfused, in 40 independent dialysis sessions, with this method during the heparin-free hemodialysis protocol without any significant difficulty. This technique only requires the addition of a stopcock and additional attention by the nursing staff to the venous pressure during the transfusion. Since no heparin hemodialysis requires one—to—one or at least one—to—two nursing, this was not found to be a problem. All 27 patients successfully completed this transfusion protocol without a need to resort to heparin. No treatments were aborted. Thus, one of the principle drawbacks with the heparin free dialysis can be resolved by a simple protocol modification as described here. We are unsure why we were more successful with this modification of our heparin free protocol as compared with our inintial study [3]. Our current success rate with the original protocol without resorting to heparin is now 95%. Thus, as we continue to use this protocol modification we anticipate a need to use low dose heparin in only a small percentage of patients.

Acknowlegement

We acknowledge the participation, skill, and perseverance of the nurses of the Duke University Acute Dialysis Program, without whose attention to improvements in patient care this study would not have been possible.

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